

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims presented in the above-identified application:

Listing of Claims:

1. (Currently amended) A system for assaying one or more targets in a sample comprising:

(a) an assay device having one or more assay sets[,,,]; each of the assay sets comprising at least two electrodes, a substrate, and a recognition moiety[,,,], the at least two electrodes positioned on the substrate and separated by a gap[,,,], the recognition moiety positioned in the gap and bound to the substrate, and the recognition moiety ~~being~~ capable of specific binding to a component of [[a]] one of the one or more targets, wherein the one of the one or more targets is selected from the group consisting of a bacterium, a virus, and a cell;

(b) an electric or electronic module arranged and configured to measure electric conductance between the at least two electrodes of ~~each~~ at least one of the one or more assay sets;

(c) ~~reagents formulated to deposit a conductive substance onto a complex formed between said recognition moiety and said target, wherein the reagents comprise: (i) a solution comprising nucleation-center forming entities for capable of binding to components of said one or more targets, if said target is present in the sample; and (ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance on said entities, and wherein the conductive substance, when deposited onto the complex, forms a conductive bridge between the at least two electrodes of a set; and~~

(d) means for determining whether at least one of the one or more targets are in the sample as a result of the extent of electric conductance between the respective at least two electrodes of ~~each~~ at least one of the one or more assay sets,

wherein the system is adapted to allow combination of the assay device, the sample, and the reagents, wherein a respective component and a respective one of the recognition moieties form a respective complex if the respective component is present in the sample and the nucleation-center forming entities can bind to the one or more targets; and in the presence of the metal ions and the reducing agent, metal is deposited on the nucleation-center forming entities on the respective complex and the deposited metal can form a conductive bridge between the respective at least two electrodes, and

wherein the metal ions in the presence of the reducing agent on the assay device are metastable so that metal deposition does not take place unless at least one of the nucleation-center forming entities is present.

2 – 3. (Canceled)

4. (Previously presented) A system according to Claim 1, wherein said nucleation-center forming entities are colloid particles.

5. (Previously presented) A system according to Claim 1, wherein said nucleation-center forming entities are metal complexes, clusters, or complexes and clusters.

6. (Original) A system according to Claim 4, wherein said colloid particles are colloid gold particles.

7. (Previously presented) A system according to Claim 5, wherein said metal complexes or clusters are gold complexes or gold clusters.

8. (Original) A system according to Claim 4, wherein said colloid particles are colloid platinum particles.

9. (Previously presented) A system according to Claim 5, wherein said metal complexes or clusters are platinum complexes or platinum clusters.

10 – 17. (Canceled)

18. (Currently amended) A system according to Claim 1, comprising a plurality of assay sets ~~of electrodes~~.

19. (Currently amended) A system according to Claim 18, wherein the respective recognition moiety in each respective assay set is capable of specific binding to a type of the component of one of the one or more targets that is the same as the component that every other one of the recognition moieties is capable of specific binding with ~~all assay sets of electrodes are for assaying the same component of the same target.~~

20. (Original) A system according to Claim 18, wherein ~~different a first~~ respective assay set or a first group of respective assays sets includes a respective recognition moiety capable of specific binding to the respective component of a first one of the one or more targets, and a second assay set or second group of assays sets

~~includes a respective recognition moiety capable of binding the respective component of a second one of the one or more targets~~ assay sets of electrodes or different groups of assay sets are for assaying different targets.

21. (Canceled)

22. (Currently amended) A system according to Claim 1, ~~when wherein at least one of the target~~ wherein at least one of the respective components is a protein or polypeptide and at least one of the respective recognition moiety moieties is a protein-binding molecule, which specifically binds to the ~~target~~ protein or polypeptide.

23. (Currently amended) A system according to Claim 22, wherein said respective recognition moiety is an antibody or antibody fraction comprising at least the antigen-binding domain of the antibody.

24. (Currently amended) A method for assaying the presence or absence of one or more biological molecule targets in a sample comprising:

(a) providing an assay device having one or more assay sets~~[[,]];~~ each of the assay sets comprising at least two electrodes, a substrate, and a recognition moiety~~[[,]];~~ the electrodes positioned on the substrate and separated by a gap~~[[,]];~~ the recognition moiety positioned in the gap and bound to the substrate, the recognition moiety ~~being~~ capable of specific binding to ~~[[a]]~~ one of the one or more biological molecule targets, wherein the ~~respective one or more biological molecule~~ targets are nucleic acid molecules and the ~~respective~~ recognition moieties are oligonucleotides, and each of the respective recognition ~~moiety~~ moieties has a

sequence which is complementary to at least a portion of ~~the a~~ respective one of the one or more biological molecule targets;

(b) ~~contacting said assay device with [[a]] the sample which may or may not have the target~~ under conditions permitting binding of the one or more biological targets, if any, present in the sample to ~~specific~~ respective recognition moieties specific for the respective ones of the one or more biological targets to form ~~a complex~~ respective complexes;

(c) contacting the assay device with a first reagent solution containing nucleation-center forming entities that can deposit onto or bind to the respective complexes;

[[(c)]] (d) contacting said assay device with metal ions and reducing agent ~~reagents to deposit a conductive substance onto the complex formed between said recognition moiety and said target,~~ such that ~~the a metal~~ conductive substance deposits onto the respective complexes if one or more of the nucleation-center forming entities is present and forms a conductive bridge between respective ones of said at least two electrodes, wherein the metal ions in the presence of the reducing agent on the assay device are metastable so that metal deposition does not take place unless one or more of the nucleation-center forming entities is present;

[[(d)]] (e) connecting respective ones of said at least two electrodes to an electric or electronic module to measure conductance between the respective ones of said at least two electrodes; and

[[(e)]] (f) determining conductance between the respective ones of said at least two electrodes, wherein conductance above a threshold conductance indicates the presence of [[a]] the respective one of the one or more biological molecule targets in the sample while conductance below [[a]] or at the threshold conductance

indicates the absence of the respective one of the one or more biological molecule targets ~~any targets~~ in the sample.

25. (Currently amended) A method for assaying the presence or absence of one or more biological molecule targets in a sample comprising;

(a) reacting a sample which may or may not have at least one of the one or more biological molecule targets with a first reagent solution to bind ~~nucleation center-forming entities~~ nucleation-center forming entities to said one or more biological targets;

(b) providing an assay device having one or more assay sets[~~l~~]; each of the assay sets comprising at least two electrodes, a substrate, and a recognition moiety[~~l~~]; the at least two electrodes positioned on the substrate and separated by a gap[~~l~~]; the recognition moiety positioned in the gap and bound to the substrate, the recognition moiety ~~being~~ capable of specific binding to [~~a~~] one of the one or more biological molecule targets;

(c) contacting said assay device with said sample which may or may not have the one or more biological molecule targets under conditions permitting binding of the one or more biological molecule targets, if any, present in the sample to specific ones of the respective recognition moieties to form respective complexes;

(d) contacting said device with a second reagent ~~solution~~ including metal ions and a reducing agent to deposit metal on a the respective complexes if one or more of the nucleation-center forming entities is present and form a conducting metal substance over said ~~nucleation-center-forming entities~~ nucleation-center forming entities for a time sufficient to yield a conductive bridge between said at least two electrodes, wherein the metal ions in the presence of the reducing agent

on the assay device are metastable so that metal deposition does not take place unless a nucleation-center forming entity is present;

(e) connecting respective ones of said at least two electrodes to an electric or electronic module to measure conductance between the respective ones of said at least two electrodes; and

(f) determining conductance between the respective ones of said at least two electrodes, wherein conductance above a threshold conductance indicates the presence of a respective one of the one or more biological molecule targets in the sample while conductance below [[a]] or at the threshold conductance indicates the absence of [[any]] the respective one of the one or more biological molecule targets in the sample.

26. (Currently amended) A method for assaying the presence or absence of one or more biological molecule targets in a sample comprising:

(a) reacting the sample with a first reagent solution containing nucleation-center forming entities that can bind to the one or more biological molecule targets if present in the sample, wherein the nucleation-center forming entities can also bind monomers of a conductive polymer;

[[a)] (b) providing an assay device having one or more assay sets[[,]; each of the assay sets comprising at least two electrodes, a substrate, and a recognition moiety[[,]; the at least two respective electrodes positioned on the substrate and separated by a gap[[,]; the recognition moiety positioned in the gap and bound to the substrate, the recognition moiety being capable of specific binding to [[a]] one of the one or more biological molecule targets;

[[b)] (c) contacting said assay device with [[a]] the sample, which may or may not have one of the one or more biological molecule ~~the~~ targets, under

conditions permitting binding of respective ones of the one or more biological molecule targets, if any, present in the sample to specific respective recognition moieties to form respective complexes;

[[c)] (d) contacting said assay device with a first second reagent solution comprising monomers of [[a]] the conductive polymer such that said monomers can bind to the nucleation-center forming entities complexes formed between the targets and recognition moieties;

[[d)] (e) treating said assay device such that said monomers will polymerize to form [[a]] the conducting polymer, such that ~~upon polymerization of the monomers~~ a conductive bridge between respective ones of the at least two electrodes corresponding to each respective complex of at least one set is formed; and

(e) determining a conductance between the respective ones of said at least two electrodes, wherein conductance above a threshold conductance indicates the presence of a respective one of the one or more biological molecule targets in the sample while conductance at or below [[a]] the threshold conductance indicates the absence of ~~any~~ the one of the one or more biological molecule targets in the sample.

27. (Canceled)

28. (Currently amended) ~~A method according to Claim 26, comprising after step (a)~~ A method for assaying the presence or absence of one or more biological molecule targets in a sample comprising:

(a) providing an assay device having one or more assay sets; each of the assay sets comprising at least two electrodes, a substrate, and a recognition moiety, the at least two respective electrodes positioned on the substrate and separated by a

gap, the recognition moiety positioned in the gap and bound to the substrate, the recognition moiety being capable of specific binding to one of the one or more biological molecule targets;

(b) contacting said assay device with the sample, which may or may not have the one or more biological molecule targets, under conditions permitting binding of respective ones of the one or more biological molecule targets, if any, present in the sample to specific respective recognition moieties to form respective complexes;

(c) contacting said assay device with a ~~second~~ first reagent solution containing nucleation-center forming entities that can bind to the one or more biological molecule targets, wherein the nucleation-center forming entities can also bind which can form nucleation centers for growing therefrom a conductive polymer from said monomers of a conductive polymer, such that said entities bind to said targets if the bound to said recognition moieties;

(d) contacting said assay device with a second reagent solution comprising monomers of the conductive polymer such that said monomers can bind to the nucleation-center forming entities;

(e) treating said assay device such that said monomers will polymerize to form the conducting polymer, such that a conductive bridge between respective ones of the at least two electrodes corresponding to each respective complex is formed;
and

(f) determining a conductance between the respective ones of said at least two electrodes, wherein conductance above a threshold conductance indicates the presence of a respective one of the one or more biological molecule targets in the sample while conductance at or below the threshold conductance indicates the absence of the one of the one or more biological molecule targets in the sample.

29 – 34. (Canceled)

35. (Currently amended) An electronic device for determining the presence or absence of one or more targets in a sample comprising:

an integrated circuit comprising a first group of N_1 conductors and a second group of N_2 conductors, defining between them $N_1 \times N_2$ junctions, each such junction being formed with an electronic module comprising two electrodes, each electrode linked to or defined as an integral portion of one of the conductors and supported by a common substrate, the circuit further comprises a diode or non-linear component permitting current flow through the electronic module only in the direction from the first group of conductors to the second group of conductors whereby a current flowing between one conductor of the first group to one conductor of the second group of conductors defines a single junction point between them; each pair of electrodes forming part of an assay set, each assay set having a recognition moiety for binding to a component of ~~[[a]]~~ one of the one or more targets selected from the group consisting of a bacterium, a virus, and a cell, and the recognition moiety is bound to the substrate and positioned between the electrodes;

the assay sets adapted to accept reagents formulated to deposit a conductive substance onto a respective complex formed between a respective one of said recognition moieties and a respective one of said one or more targets wherein said reagents comprise: (i) a solution comprising nucleation-center forming entities for binding to ~~components of~~ one or more targets if said one or more targets is present in the sample; and (ii) ~~a combination of~~ metal ions and a reducing agent to allow formation of said conductive substance on said nucleation-center forming entities; wherein in the presence

of the metal ions and the reducing agent, metal is deposited on the nucleation-center forming entities and the deposited metal can form a conductive bridge between respective ones of the at least two electrodes, and wherein the metal ions in the presence of the reducing agent on the assay sets are metastable so that metal deposition does not take place unless at least one of the nucleation-center forming entities is present.

and means for determining whether the one or more targets are in the sample as a result of the extent of electric conductance between the two electrodes of each assay set.

36. (Currently amended) A device according to Claim 35, wherein each of the assay sets has a center and is separated from an adjacent assay set by a distance, and the distance of the center of one assay set to a the center of an adjacent assay set is 100 μ m or less.

37. (Currently amended) An electric device for determining the presence or absence of one or more targets in a sample comprising:

a microelectronic device having a plurality of layers, with a first group of conductors being defined as stripes in one or more first layers and a second group of conductors being defined as stripes in one or more second layers of the device with each of said second layers being separated from a first layer by a non-conductive substance, electrodes of the device being formed as open ends of the conductors by openings or cut-outs in a vertical direction through the layers;

each pairs of the electrodes forming part of [[an]] assay sets[[,]]; each assay set having a recognition moiety for binding to a component of one of the one or more [[a]] targets, wherein the one of the one or more targets is selected from the group

consisting of a bacterium, a virus, and a cell ~~bound to one or more layer in the vertical opening or cut out~~; wherein the assay sets are adapted to accept reagents formulated to deposit a conductive substance onto a respective complex formed between a respective one of said recognition ~~moiety~~ moieties and a respective component ~~said target~~, wherein said reagents comprise: (i) a solution comprising nucleation-center forming entities for binding to ~~components of~~ said one or more targets if said one or more targets ~~[[is]]~~ are present in the sample; and (ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance on said ~~entities~~ nucleation-center forming entities, and

means for determining whether the one or more targets are in the sample as a result of the extent of electric conductance between the pair of electrodes of each assay set.

38. (Currently amended) A system according to Claim 18, wherein the device is an electronic device for determining one or more targets in a sample, comprising:

an integrated circuit comprising the first group of N_1 conductors and a second group of N_2 conductors, defining between them ~~the~~ $N_1 \times N_2$ junctions, each ~~such of the~~ $N_1 \times N_2$ junctions ~~being~~ formed with an electronic module comprising the at least two electrodes, each of the at least two electrodes ~~one~~ linked to or defined as an integral portion of one of the conductors, ~~and~~ ~~comprises~~ the integrated circuit further comprising a diode or non-linear component permitting current flow through the electronic module only in the direction from the first group of conductors to the second group of conductors, whereby a current flowing between one conductor of the first group of N_1 conductors to ~~the~~ one conductor of the second group of N_2 conductors defines

a single junction point between the first group of N_1 conductors the second group of N_2 conductors ~~them; each pair of electrodes forming part of an array set, each array set having a recognition moiety bound to at least one of the electrodes.~~

39. (Previously presented) A method according to Claim 24, wherein said assay device is an electronic device for determining one or more targets in a sample, comprising:

an integrated circuit comprising the first group of N_1 conductors and a second group of N_2 conductors, defining between them $N_1 \times N_2$ junctions, each such junction being formed with an electronic module comprising the at least two electrodes, each electrode linked to or defined as an integral portion of one of the conductors ~~and supported by a common substrate~~, the integrated circuit further comprises comprising a diode or non-linear component permitting current flow through the electronic module only in the direction from the first group of conductors to the second group of conductors, whereby a current flowing between one conductor of the first group of N_1 conductors to one conductor of the second group of N_2 conductors defines a single junction point between the first group of N_1 conductors and the second group of N_2 conductors ~~them; each pair of electrodes forming part of an array set, each array set having a recognition moiety bound to the substrate and positioned between the electrodes.~~

40. (Canceled)

41. (Currently amended) A method for detecting the presence or absence of one or more targets in a sample by multiplexing comprising:

(i) contacting the electronic device of Claim 35 with a sample which may or may not have the one or more targets under conditions enabling binding of the one or more targets, if any, present in the sample to the recognition moieties; and

(ii) determining conductance in each assay set.

42. (Canceled)

43. (Previously presented) A system according to Claim 1, wherein said one or more targets are one or more nucleic acid sequences.

44. (Currently amended) A system according to Claim 43, wherein said recognition moiety is an oligonucleotide having a sequence complementary to at least a portion of ~~sequence of~~ one of said one or more targets.

45 – 46. (Canceled)

46. (Canceled)

47. (Currently amended) A method according to Claim 25, wherein said one or more biological molecule targets are nucleic acid molecules and the recognition moieties are oligonucleotides, ~~each of which has a sequence which is complementary to a nucleic acid molecule of said target.~~

48. (Currently amended) A method according to Claim 26, wherein said one or more biological molecule targets are nucleic acid molecules and the recognition moieties are oligonucleotides, ~~each of which has a sequence which is complementary to a nucleic acid molecule of said target.~~

49. (Currently amended) A method according to Claim 24, wherein said one of the one or more biological molecule targets ~~are~~ is selected from the group consisting of a bacterium component, a virus component, and a cell component.

50. (Currently amended) A method according to Claim 25, wherein said one of the one or more biological molecule targets ~~are~~ is selected from the group consisting of a bacterium component, a virus component, and a cell component.

51. (Currently amended) A method according to Claim 26, wherein said one of the one or more biological molecule targets ~~are~~ is selected from the group consisting of a bacterium component, a virus component, and a cell component.

52. (Canceled)

53. (Previously presented) An electronic device according to Claim 35, wherein said recognition moiety is a nucleic acid molecule.

54. (Previously presented) An electric device according to Claim 37, wherein said recognition moiety is a nucleic acid molecule.

55. (Previously presented) A system according to Claim 1, wherein said means comprises a computer.

56. (Previously presented) A system according to Claim 1, wherein said means comprises a scanner for analyzing a plurality of assay sets.

57. (Previously presented) A system according to Claim 1, further comprising a sample which may or may not have the target.

58 – 59. (Canceled)

60. (Previously presented) An electronic device according to Claim 35, wherein said means comprises a computer.

61. (Previously presented) An electronic device according to Claim 35, wherein said means comprises a scanner for analyzing a plurality of assay sets.

62. (Previously presented) An electric device according to Claim 37, wherein said means comprises a computer.

63. (Previously presented) An electric device according to Claim 37, wherein said means comprises a scanner for analyzing a plurality of assay sets.

64. (Canceled)

65. (Currently amended) A system for assaying one or more targets in a sample comprising:

(a) an assay device having one or more assay sets, each of the assay sets comprising at least two electrodes and a recognition moiety immobilized to each of the at least two electrodes, each recognition moiety being an antibody capable of specific binding to an epitope of [a] one of the one or more targets, wherein the one of the one or more targets is selected from the group consisting of a bacterium, a virus, and a cell;

(b) an electric or electronic module arranged and configured to measure electric conductance between the at least two electrodes of each assay set;

(c) reagents formulated to deposit a conductive substance onto a respective complex formed between a respective said recognition moiety and a respective one of said one or more targets, wherein the reagents comprise: (i) a solution comprising nucleation-center forming entities for binding to components of said one or more targets if said one or more targets [is] are present in the sample; and (ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance on said entities, and wherein the system is adapted to allow the combination of the assay device, the sample, and the reagents, and in the presence of the metal ions and the reducing agent, metal is deposited on the nucleation-center forming entities and the deposited metal can form a conductive bridge between the respective at least two electrodes, and wherein the metal ions in the presence of the reducing agent on the assay sets are metastable so that metal deposition does not take place unless a nucleation-center forming entity is present the conductive substance, when deposited onto the complex, forms a conductive bridge between the at least two of the electrodes of a set; and

Applicant: Eichen et al.
Application No.: 09/674,090

(d) a computer for determining whether the one or more targets are in the sample as a result of the extent of electric conductance between the at least two electrodes of each assay set.

66. (Canceled)